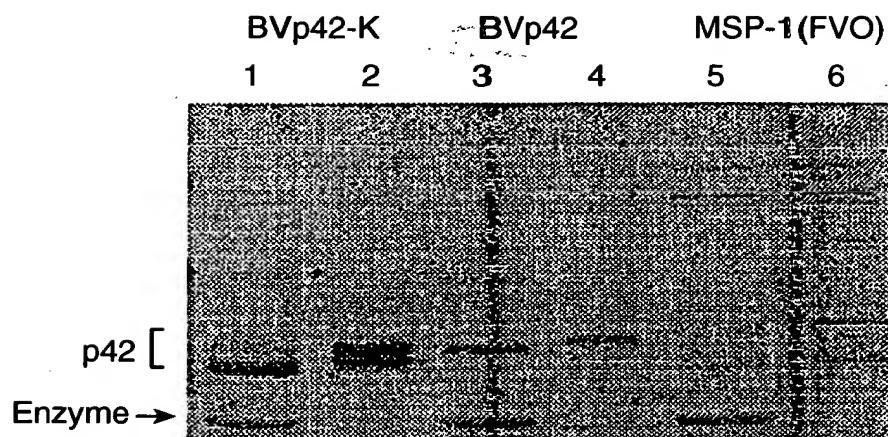
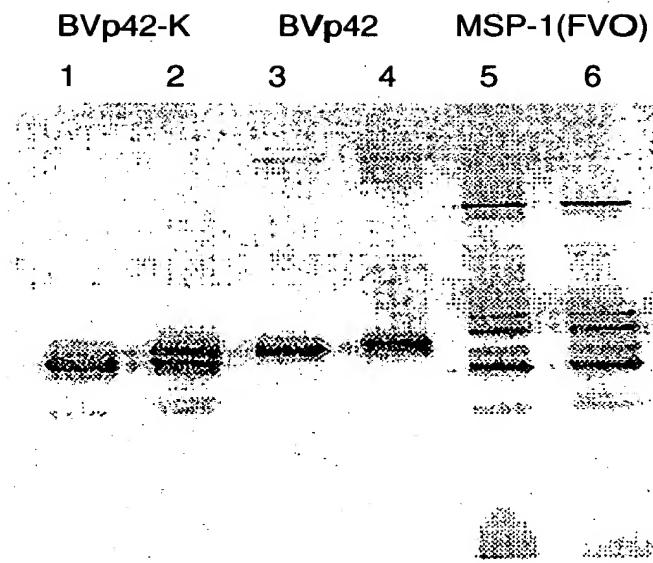
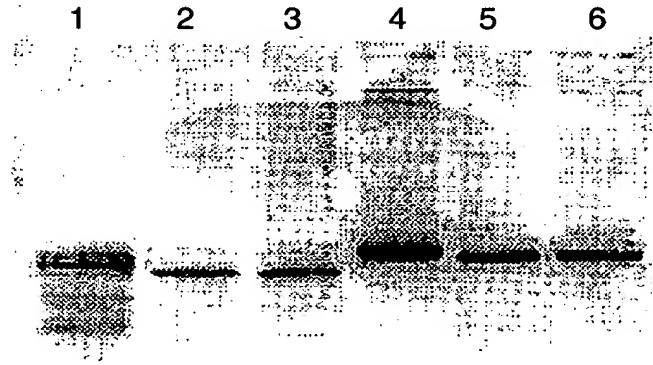


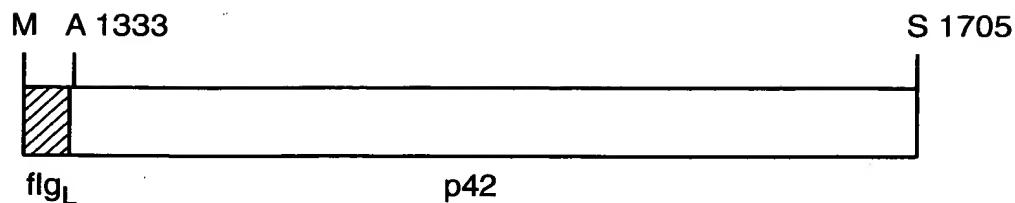
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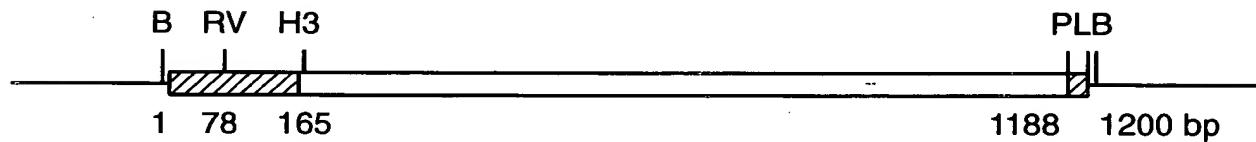
**FIG.\_19A****FIG.\_19B****FIG.\_20**

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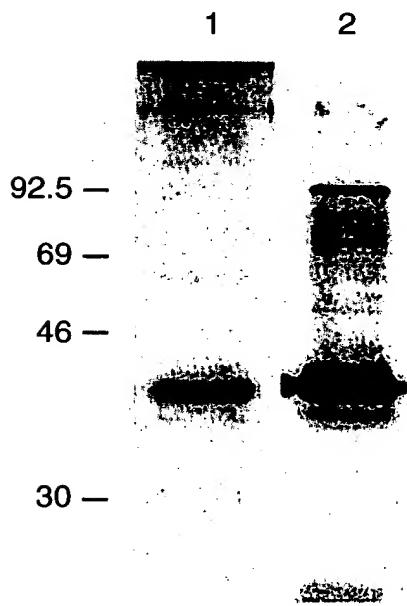
102504



**FIG. 1A**



**FIG. 1B**



**FIG.-2A**

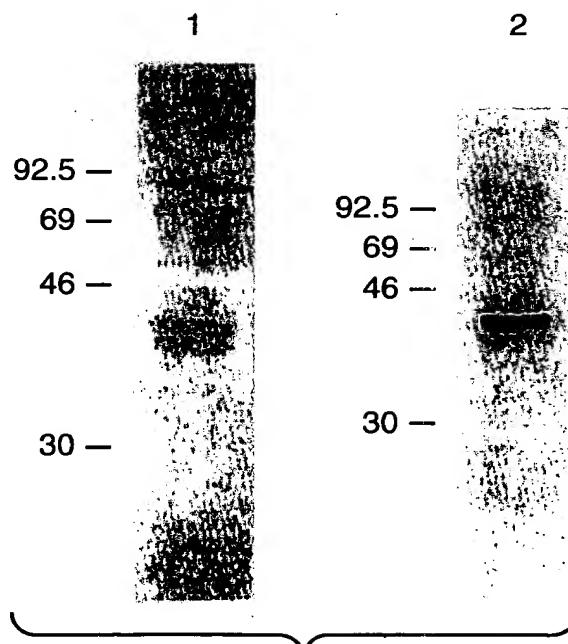
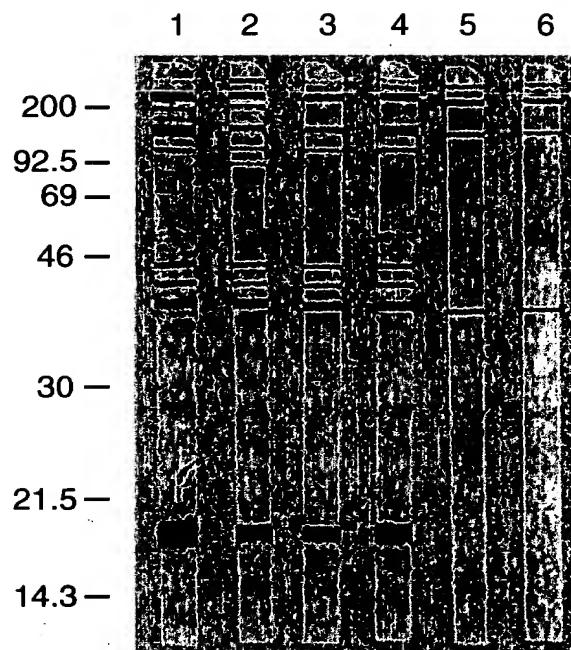
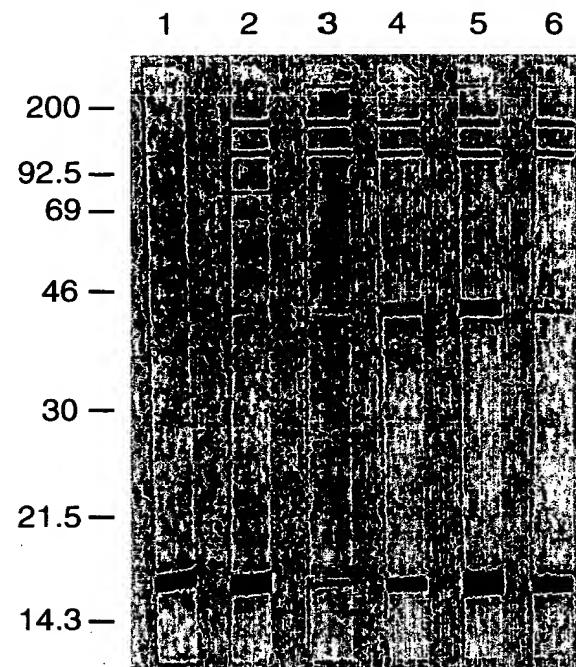
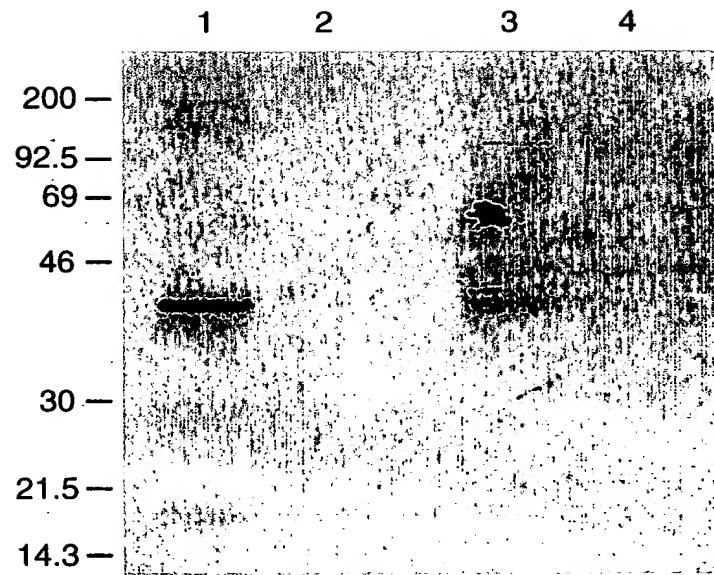


FIG.-2B

17698 U.S.PTO  
102504**FIG. 3A****FIG. 3B****FIG. 3C**

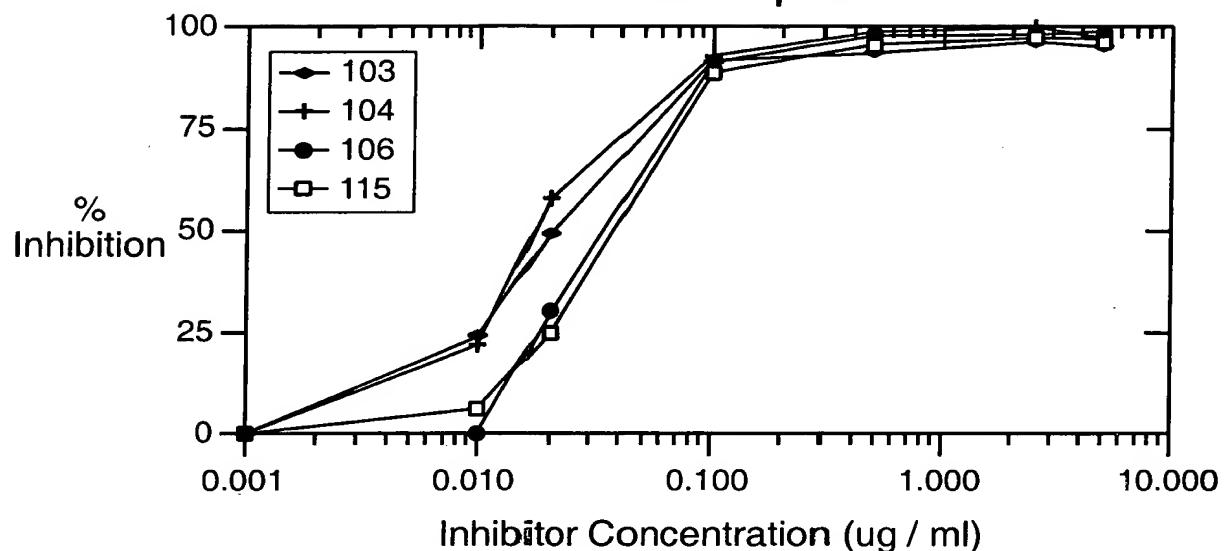
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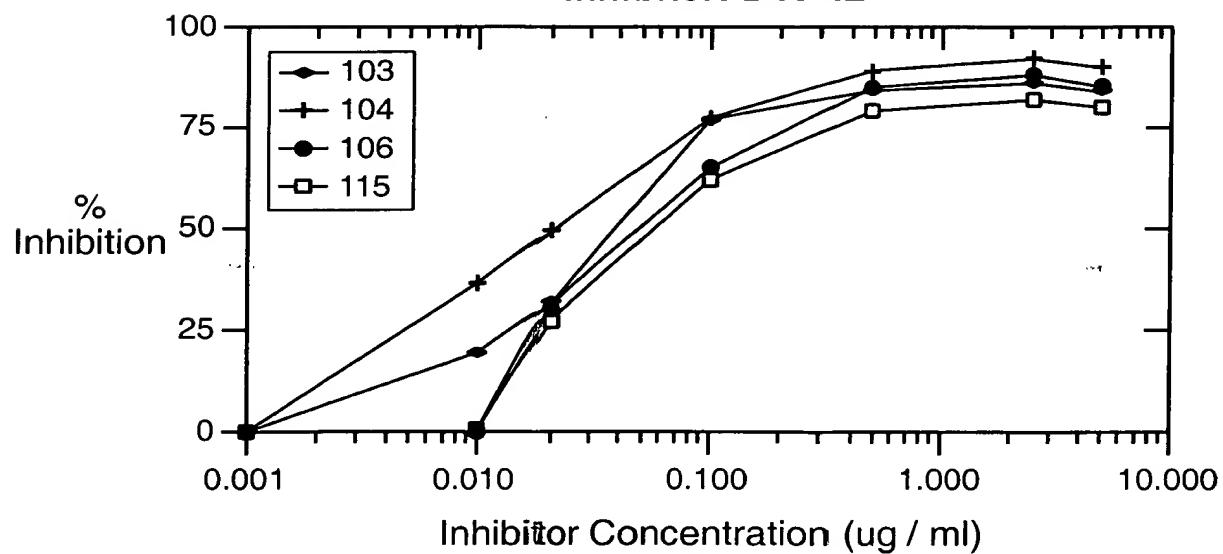


**Inhibitor: Gp195**



**FIG.\_4A**

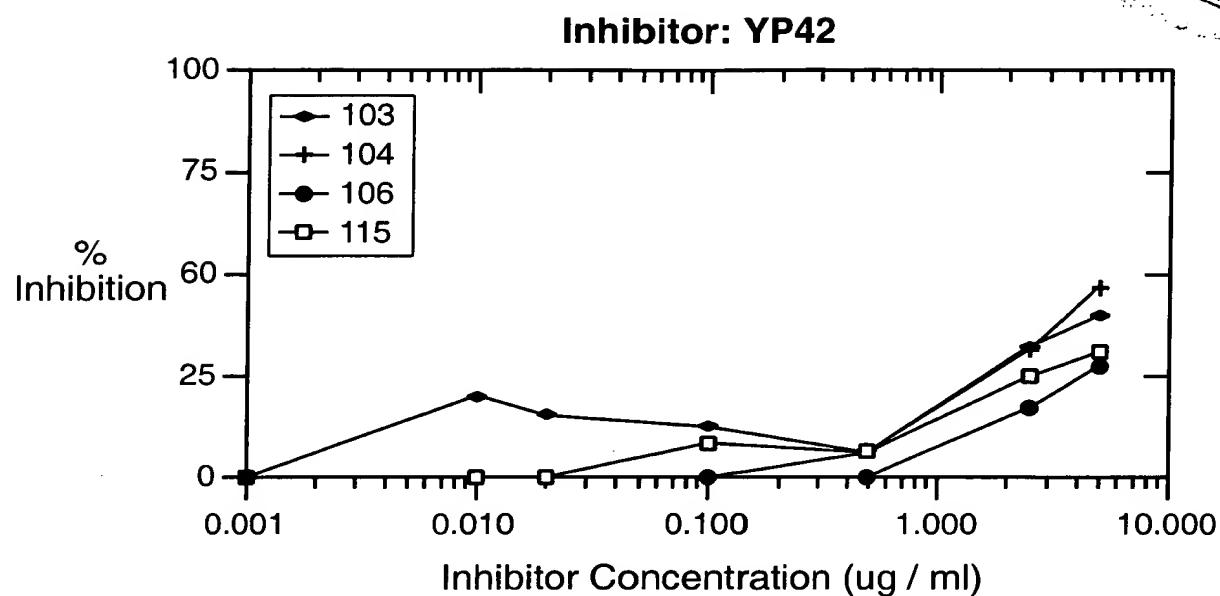
**Inhibitor: BVP42**



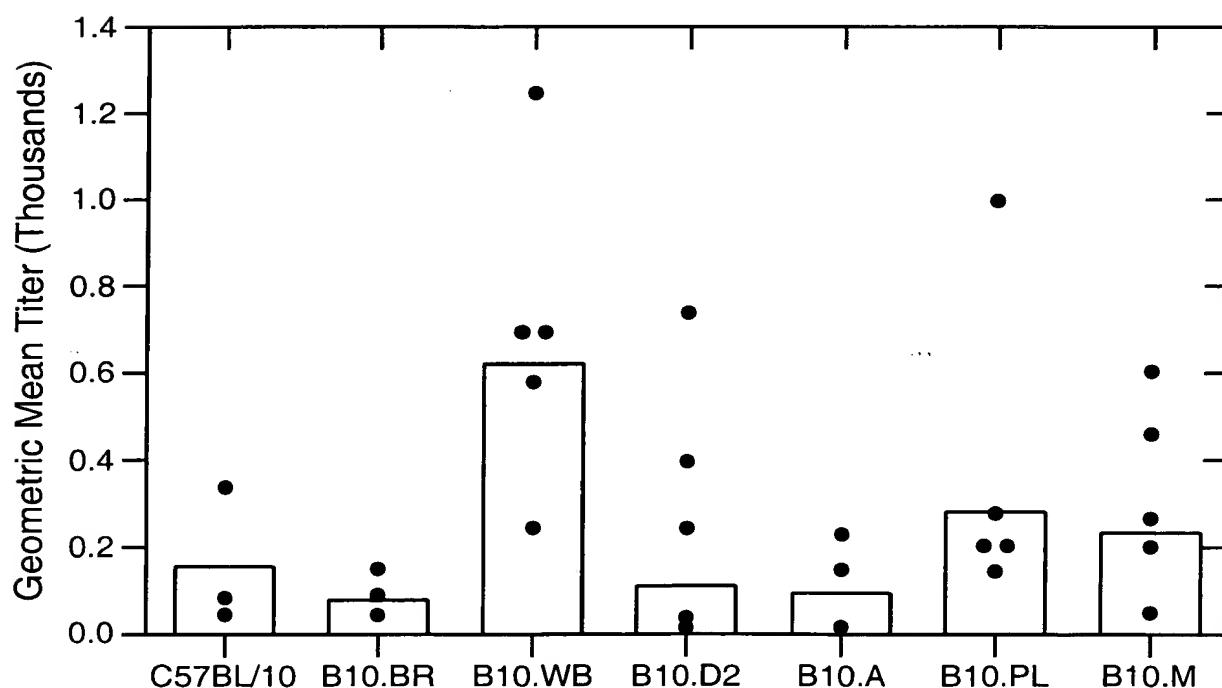
**FIG.\_4B**

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**FIG.\_4C**



**FIG.\_5**

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|     |  |                        |
|-----|--|------------------------|
| FUP | AISVT.MDNILSGFENNEYDVYLKPLAGVYRSILKQIEKNIFTFNILNLILNSRLKIRKYFLDVLESILM | 1402                   |
| MAD |  |                        |
| WEL | KI E L   | I                      |
| K1  | VTPSVIH KI E L   | L N VM V VK FN EN KN I |
|     |  | 1377                   |
|     |  | 1384                   |
|     |  | 1325                   |

|     |   |      |
|-----|---|------|
| FUP | QFKHISNEYIILEDOSFKILNSEQNKNTLLKSRYIKESVENDIKRFAQEGISYYEKVLAKYKODLESIKKVIK | 1473 |
| MAD |   |      |
| WEL | PY DLT SN VVK PY F K KRDKF S N D IDT N NDVLG KILSE S D Y N                | 1448 |
| K1  | PY DLT SN VVK PY F K KRDKF S N D IDT N NDVLG KILSE S D Y N                | 1405 |
|     |   | 1396 |

|     |   |      |
|-----|---|------|
| FUP | EEKEKEFPSSPPTTPSPAKTDEQKKESKFLPFLTNIETLYNNLYNKDDYLINLAKAKINDCVERKDEAHVK | 1544 |
| MAD |   |      |
| WEL | ..... K GENE Y N KTVND LFV H E VLNNTY SNVE                              | 1519 |
| K1  | ..... K GENE Y N KTVND LFV H E VLNNTY SNVE                              | 1456 |
|     |   | 1447 |

|     |   |      |
|-----|---|------|
| FUP | ITKLSDLKAIDDKIDLTKNHNDPEAIKKLINDDTKDKULGKLLSTGLV.QNFPTNTIISKLIEGKFQDMIL.N | 1613 |
| MAD |   |      |
| WEL | KE NY T Q LAD KN N VG AD ST YNHNNL T F M FE LIKSVL N LDW LARYVKH          | 1588 |
| K1  | KE IY T Q LAD KN N VG AD ST YNHNNL T F M FE LIKSVL N LDW LARYVKH          | 1527 |
|     |   | 1518 |

|     |   |      |
|-----|---|------|
| FUP | ISQHQCVKKQCPENSFCFRHLDERECKCLNYKQEGDKCVENPNPTCNEENGGCCADAKCTEEDSGSNGK | 1684 |
| MAD |   |      |
| WEL | FTTPMRK TMIQQS E T SR   | 1659 |
| K1  | FTTPMRK TMIQQS S  | 1598 |
|     |   | 1589 |

|     |  |      |
|-----|--|------|
| FUP | KITCECTKPDSYPLFDGIPCSSSNFLGISFLLILYLISFI | 1726 |
| MAD |  |      |
| WEL | Q C SHV                                  | 1701 |
| K1  |  | 1640 |
|     |  | 1631 |

FIG.-6



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BAMHI | | | HIND3 | | | AFL2 | | | AHA3  
 ECORV | | | HIND3 | | | AFL2 | | | AHA3  
 SAC2 AHA3 AHA3 AHA3 AHA3  
 ECORV | | | ECORV | | | ECORI  
 SSPI

PAC1

AHA3 | | | ASE1 | | |  
 BGL2 | | |  
 AHA3 | | |  
 ASU2 | | |  
 BSTB1 | | |  
 BSAB1  
 PSTI  
 SALI  
 BAMHI

Met Trp Ser Trp Lys Cys Leu Leu Phe Trp Ala Val Leu Val Thr Ala  
 1 GGATCCACTGGGATGTGGAGCTGGAAAGTGCCTCCTCTGGCTGTCACAGCC  
 CCTAGGTGACCCCTACACCTCGACCTCACGGAGGAGAACCGACAGGACCAAGTGTCCG  
 1 BAMHI,  
 Thr Leu Cys Thr Ala Ala Ile Ser Val Thr Met Asp Asn Ile Leu Ser Gly Phe Glu Asn  
 61 ACACTCTGCACCGCGCGATATCTGTACAATGGATAATATCCTCAGGATTGAAAAT  
 TGTGAGACGTGGCGCCGCTATAGACAGTGTACCTATTATAGGAGAGTCCTAAACTTTA  
 71 SAC2, 78 ECORV,  
 Glu Tyr Asp Val Ile Tyr Leu Lys Pro Leu Ala Gly Val Tyr Arg Ser Leu Lys Lys Gln  
 121 GAATATGATGTTATATATTAAACCTTAGCTGGAGTATAGAACGCTTAAAAACAA  
 CTTATACTACAATATATAATTTGGAAATCGACCTCATATATCTCGAATTTTTGTT  
 138 AHA3, 165 HIND3,  
 Ile Glu Lys Asn Ile Phe Thr Phe Asn Leu Asn Asp Ile Leu Asn Ser Arg Leu  
 181 ATTGAAAAAACATTTCATTTAACATTGAAAGATATCTAAATTACGTCTT  
 TAACCTTTTGTAATGTAATTAAACTTGCTATAGAATTAAAGTGCAGAA  
 207 AHA3, 220 ECORV, 238 AFL2,  
 Lys Lys Arg Lys Tyr Phe Leu Asp Val Leu Glu Ser Asp Leu Met Gln Phe Lys His Ile  
 241 AAGAAACGAAATATTCTTAGATGTATTAGAACATTGCAATTAAACATATA  
 TTCTTGCTTTATAAGAACATCTACATAATCTTAGACTAAATTACGTTAAATTGTATAT  
 251 SSPI, 289 AHA3,  
 Ser Ser Asn Glu Tyr Ile Ile Glu Asp Ser Phe Lys Leu Leu Asn Ser Glu Gln Lys Asn

**FIG.\_7A**



301 TCCTCAAATGAATACTTATTGAAGATTCA~~TTAA~~ATTGAATTCA~~GAA~~ACAAAAAAAC  
 AGGAGTTACTTATGTAATAACTCTAAGTAATTAATAACTTAAGTCTGTTTTTG  
 331 AHA3, 342 ECORI,  
 361 ThrLeuLeuLysSerTyrLysTyrIleLysGluSerValGluAsnAspIleLysPheAla  
 ACAC~~TTT~~AAAAAGTTACAAATATATAAGAATCAGTAGAAATGATATTAAATTGCA  
 TGTAATTTCAATGTTATATATTCTTAGTCATCTTACTATAATTAAACGT  
 366 AHA3,  
 421 GlnGluGlyIleSerTyrTyrGluLysValLeuAlaLysTyrLysAspAspLeuGluSer  
 CAGGAAGGTATAAGTTATTATGAAAGGTTAGCGAAATATAAGGATGATTAGAATCA  
 GTCCTTCCATATTCAATAACTTTCCAAATCGCTTATTCCTACTAAATCTTAGT  
 481 IleLysLysValIleLysGluGluLysGluLysPheProSerSerProProThrThrPro  
 ATTAAAAAGTTATCAAAGAAAGAAAGGGAGTTCCCATCATCACCAACAAACACT  
 TAATTTTTCAATAGTTCTCTTCCCTTCAGGGTAGTAGTGGTGGTTGTGGGA  
 541 ProSerProAlaLysThrAspGluGlnLysLysGluSerLysPheLeuProPheLeuThr  
 CCGTCACCAGCAAAACAGACGAACAAAGGAAGGAAGGTAAAGTTCCCTCCATTAACA  
 GGCAGTGGTCGTTTGCTGCTGTTCTCCTTCATTCAAGGAAGGTAAAATTGT  
 601 AsnIleGluThrLeuTyrAsnAsnLeuValAsnLysIleAspAspTyrLeuIleAsnLeu  
 AACATTGAGACCTTATACAATAACTTAGTTAATAAAATTGACGATTACTTAATTAACTTA  
 TTGTAACTCTGAATATGTTATTGAATCAATTATTTACTGCTAATGAATTAATTGAAT  
 649 PAC1,  
 661 LysAlaLysIleAsnAspCysAsnValGluLysAspGluAlaHisValLysIleThrLys  
 AAGGCAAAGATTAACGATTGTAATGTTAAAGATGAAGCAATGTTAAAAACTAA  
 TTCCGTTCTAATTGCTAACATTACAACTTTCTCGTGTACATTGATTTATTGATT  
 721 LeuSerAspLeuLysAlaIleAspAspLysIleAspLeuPheLysAsnHisAsnAspPhe  
 CTTAGTGATTTAAAGCAATGTAGCAAAATAGATCTTTAAACATACGACTTC  
 GAATCACTTTAAATTTCGTTAACTACTGTTTATCTAGAAATTTGGTATTGCTGAAG  
 729 AHA3, 753 BGL2, 760 AHA3, 778 ASU2 BSTB1,  
 781 GluAlaIleLysLysLeuIleAsnAspAspThrLysAspMetLeuGlyLysLeuLeu  
 GAAGCAATTTAAATTTGATAAATGATGATACGAAAAGATATGCTGGCAATTATGA  
 CTTCGTTAATTTTAACTATTTACTATTCATGCTTTTCTATCGACCGTTATGA  
 841 SerThrGlyLeuValGlnAsnPheProAsnThrIleIleSerLysLeuIleGluGlyLys  
 AGTACAGGATTAGTTCAAAATTTCCTAATCAAATAATCAAATTGAAGAAAA  
 TCATGTCCTAATCAAGTTAAAGGATTATGTTTATATAGTTAACTCCTTTT  
 885 ASE1,  
 901 PheGlnAspMetLeuAsnIleSerGlnHisGlnCysValLysLysGlnCysProGluAsn  
 TTCCAAAGATATGTAAACATTTCCACCAATGCGTAAAAAAACATGTCCCAGAAAT  
 AAGGTTCTATTCAAGTGTGGTTACGCATTTTTGTTACAGGTCTTTTA  
 961 SerGlyCysPheArgHisLeuAspGluArgGluCysLysCysLeuLeuAsnTyrLys  
 TCTGGATGTTTCAGACATTTAGATGAAAAGAGAAATGTAAATGTTTATAAATCAAA  
 AGACCTACAAAGTCGTAAATCTACTTCTCTACATTTACAAATTAATGTTT



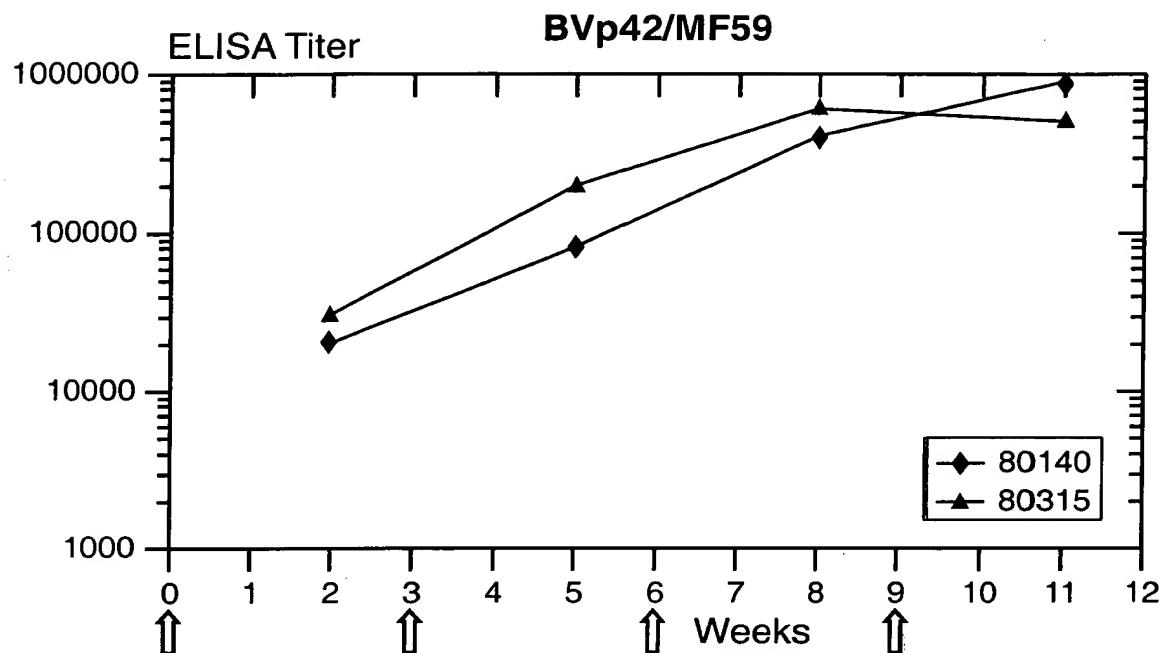
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1021 GlnGluGlyAspLysCysValGluAsnProAsnProThrCysAsnGluAsnAsnGlyGly  
 CAAGAAGGTGATAAAATGTGTTGAAAATCCAAATCCTACTTGTAAACGAAAATAATGGTGGAA  
 GTTCTTCCACTATTACACAACCTTAGGTTAGGATGAACATTGCTTTATTACCACCT  
  
 1081 CysAspAlaAspAlaLysCysThrGluGluAspSerGlySerAsnGlyLysLysIleThr  
 TGTGATGCAGATGCCAATGTACCGAAGAAGATTCAAGGTAGCAACGGAAAGAAAATCACA  
 ACACATACGTCTACGGTTACATGGCTTCTAAGTCCATCGTGCCTTCTTTAGTGT  
  
 1141 CysGluCysThrLysProAspSerTyrProLeuPheAspGlyIlePheCysSerAM AM  
 TGTGAATGTAATAACCTGATTCTTATCCACTTTCGATGGTATTTCTGCAGTTAGTAG  
 ACACTTACATGATTGGACTAAGAATAGGTGAAAAGCTACCATAAAAGACGTCAATCATC  
  
 1159 BSAB1, 1188 PSTI, 1200 SALI.  
  
 1201 TCGACCCCTGGAAGGATCC  
 AGCTGGGAACCTTCCTAGG  
  
 1214 BAMHI,  
  
 1261

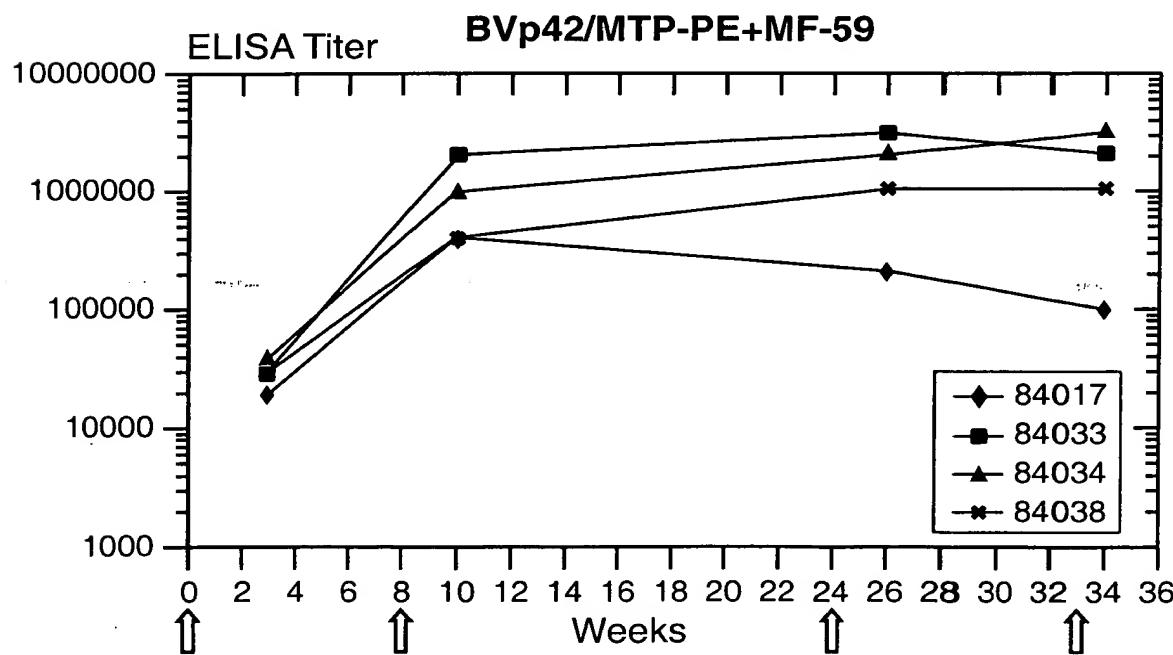
**FIG.\_7C**

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**FIG.\_8A**

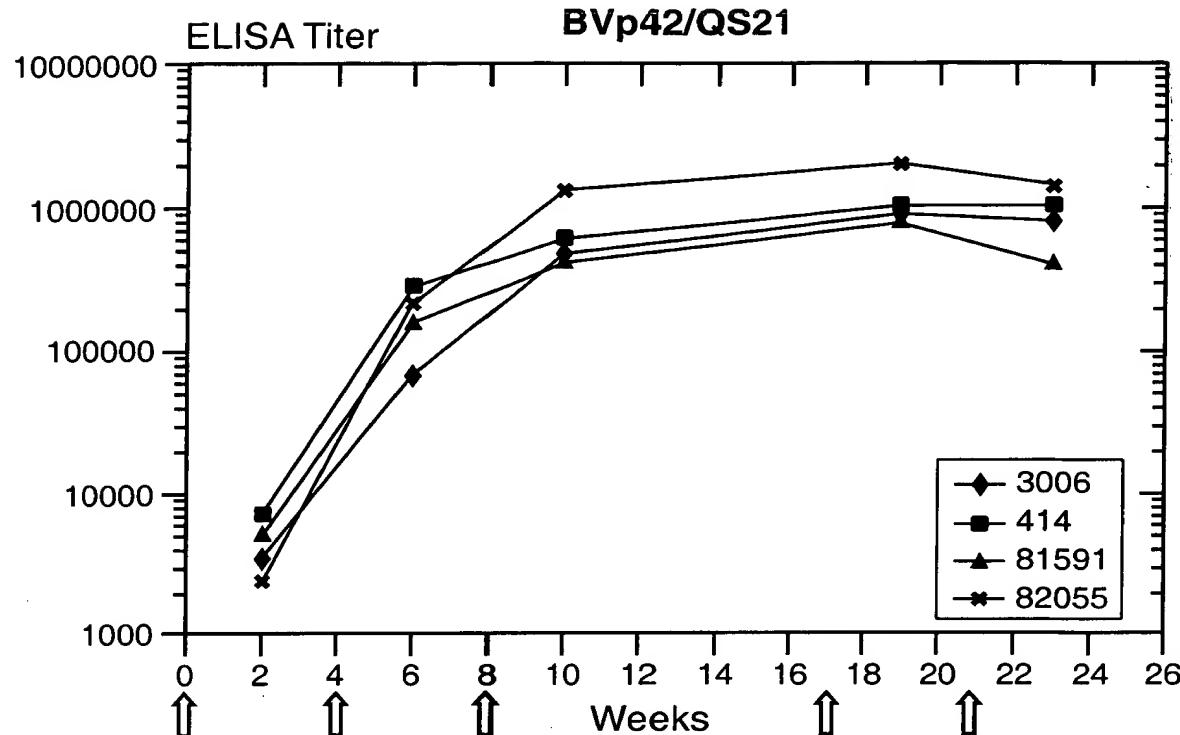
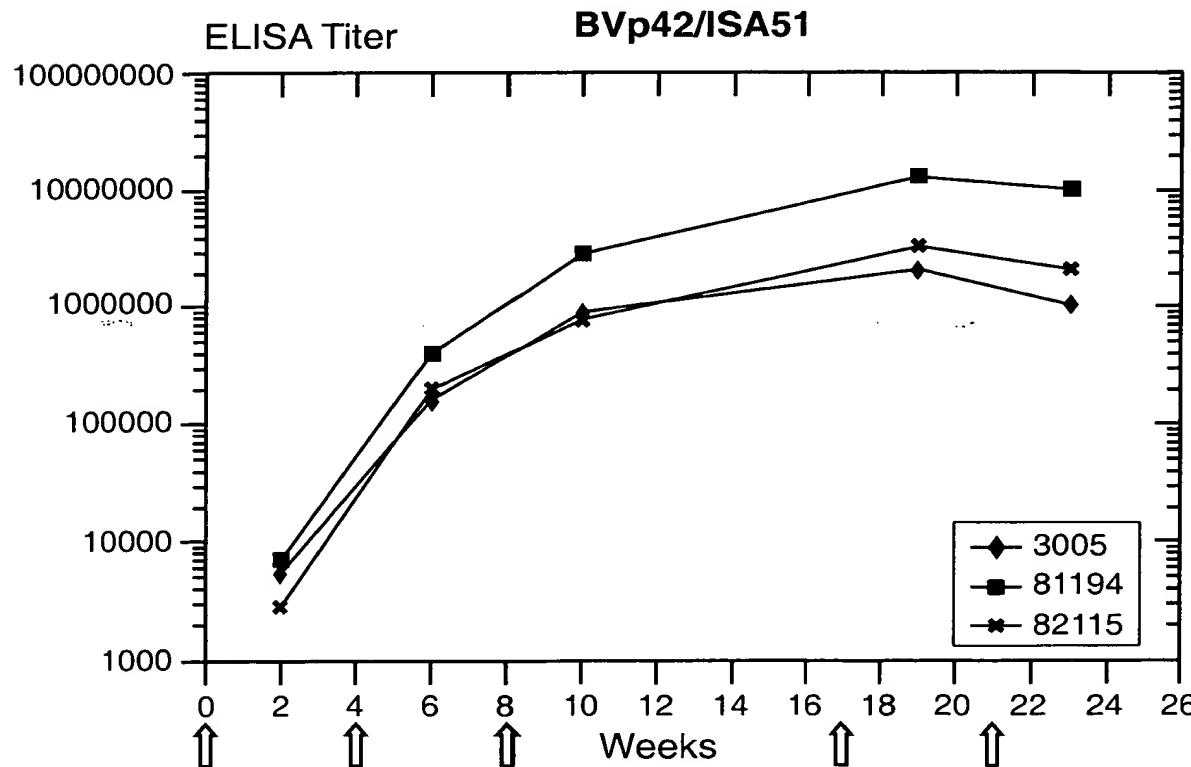


**FIG.\_8B**



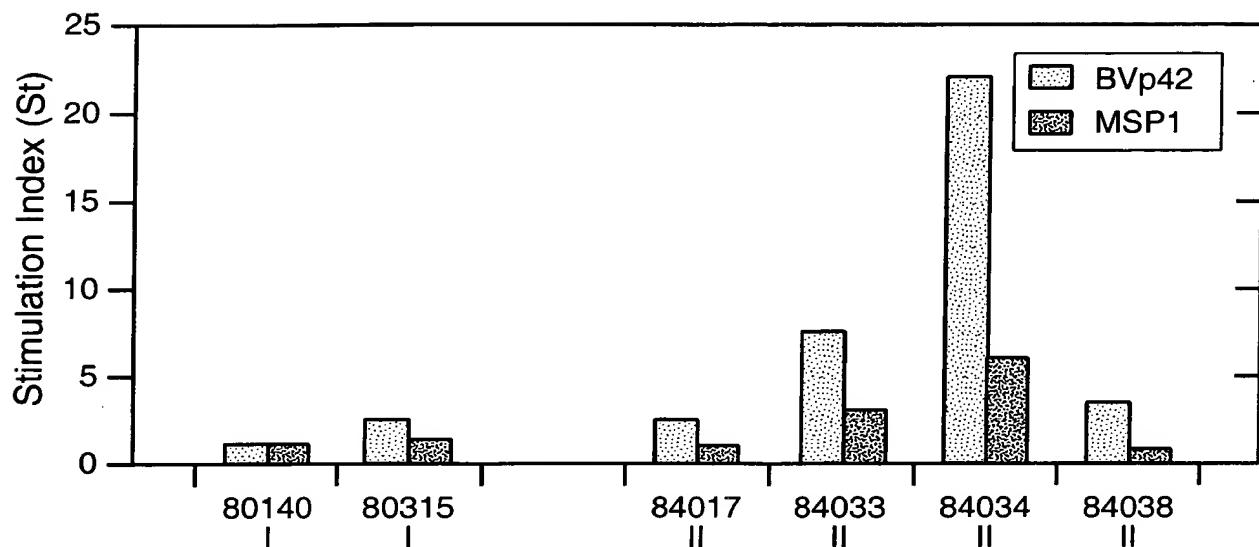
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**FIG.\_8C****FIG.\_8D**

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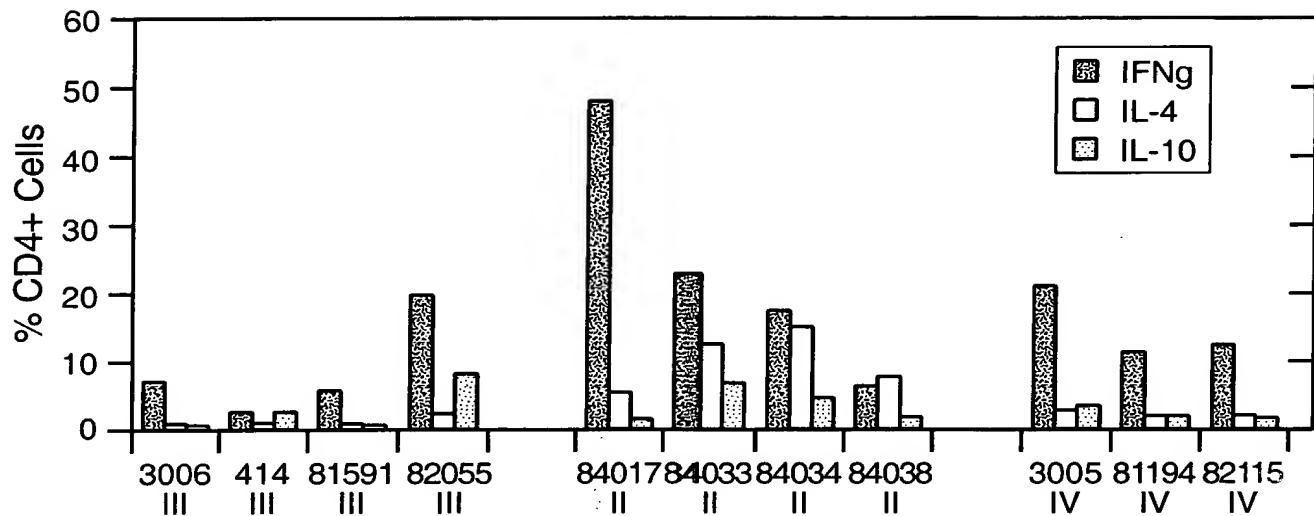
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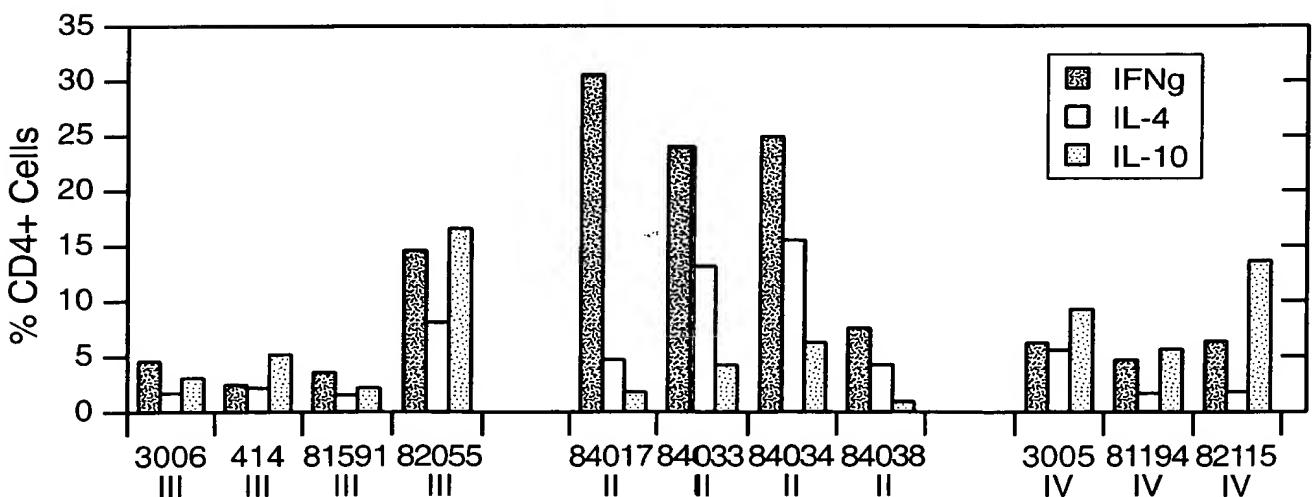
**FIG.\_9**

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**FIG.\_ 10A**



**FIG.\_ 10B**

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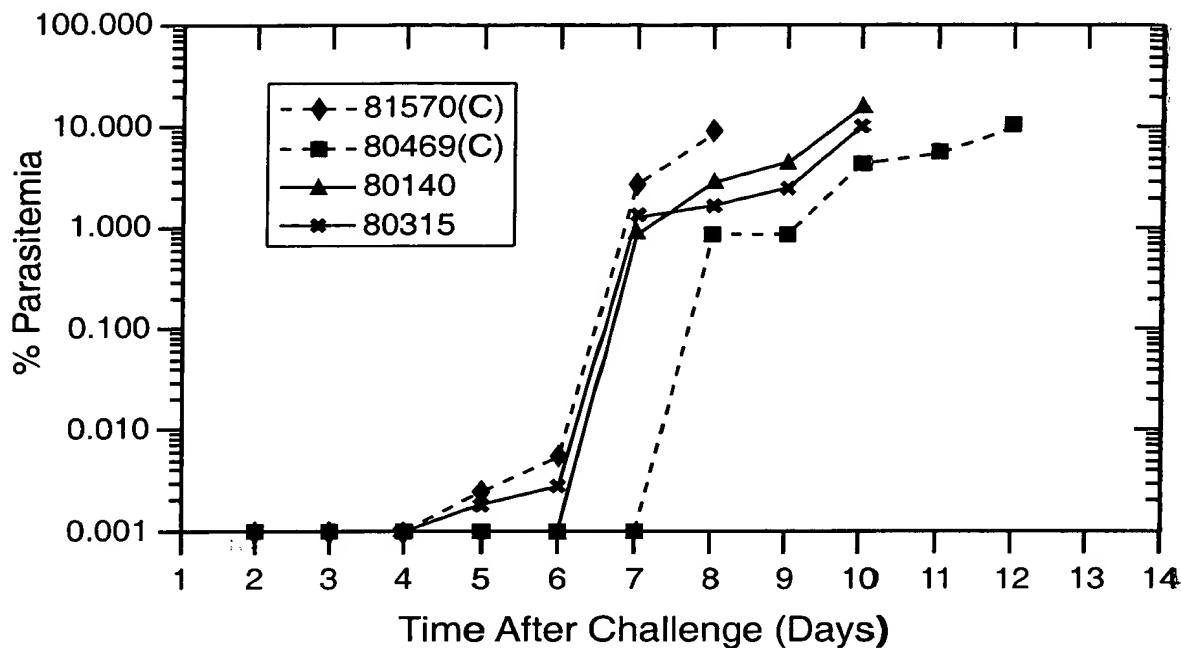


FIG. 11A

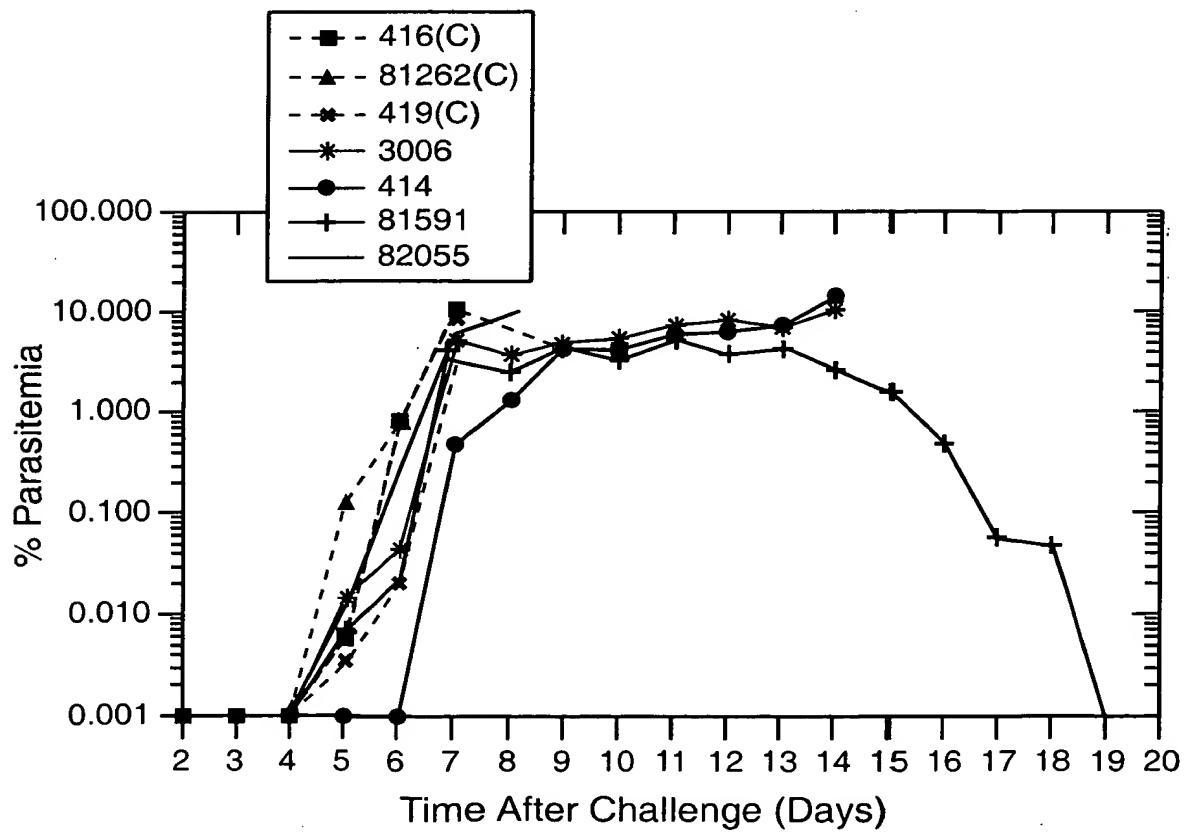


FIG. 11B

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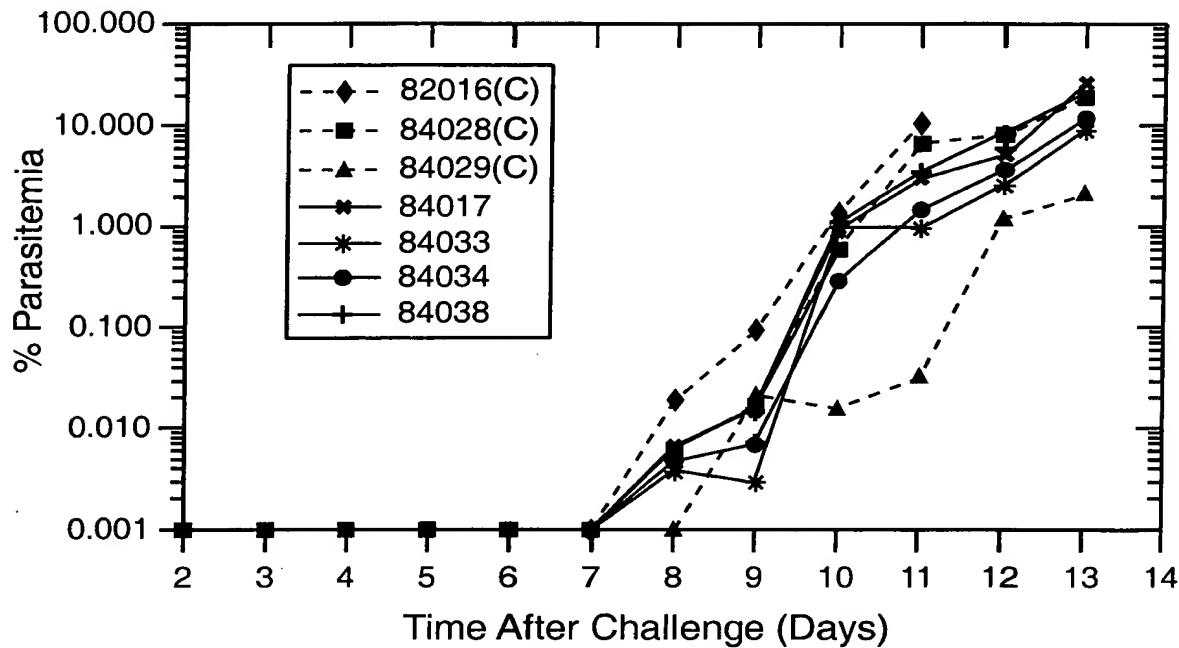


FIG.\_ 11C

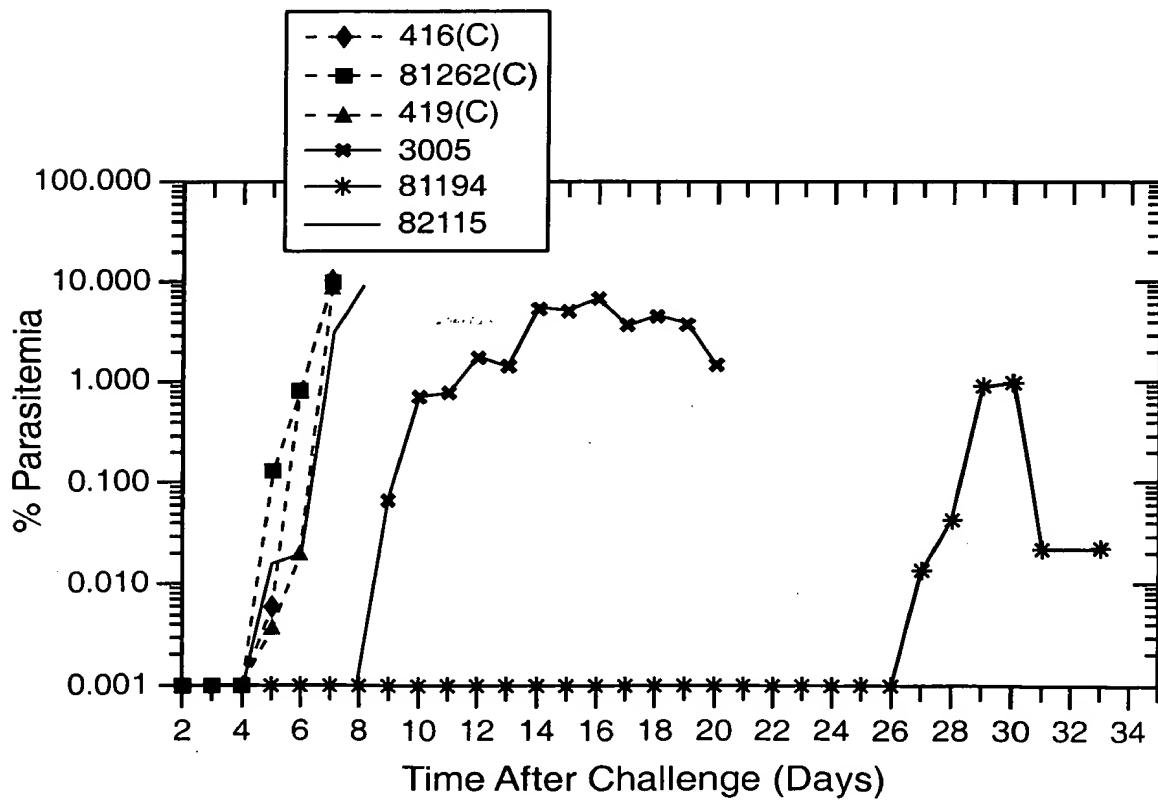


FIG. 11D

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## DNA AND AMINO ACID SEQUENCE OF BVp42-M

attggatccactaaa

13 atgtggtcttggaaagtgtctttattctgggctgtcttggtgacc  
 M W S W K C L L F W A V L V T  
 58 gccactcttgcacagcagcgtctgttactatggacaaacatc  
 A T L C T A A I S V T M D N I  
 103 ctcagtggcttcgagaacgaggtacgacgtaatctacctaagccc  
 L S G F E N E Y D V I Y L K P  
 148 ctgcgggtgtctaccgttattgaagaaacagatagaaaagaat  
 L A G V Y R S L K K Q I E K N  
 193 atttcacgttcaacctcaacctaattgacatcctcaactcgcc  
 I F T F N L N L N D I L N S R  
 238 ctcaagaagcggaaaataacttcctcgacgtgttggaatccgacctt  
 L K K R K Y F L D V L E S D L  
 283 atgcaattnaaggcacattagctctaaccgtacatcatagaggac  
 M Q F K H I S S N E Y I I E D  
 328 agcttcaagctttgaattcagaacacagaagaacaccctctaaag  
 S F K L L N S E Q K N T L L K  
 373 tcctacaaatacattaaggagtctgttggataacgacatcaagttc  
 S Y K Y I K E S V E N D I K F  
 418 gcccaggaaggaatttagctactatgagaaagtctctggctaaatac  
 A Q E G I S Y Y E K V L A K Y  
 463 aaggacgacttggaaagcattaagaaggtaatcaaagaagagaag  
 K D D L E S I K K V I K E E K  
 508 gaaaagttccgagcttcacccacaactccccatcgccctgca  
 E K F P S S P P T T P P S P A  
 553 aagaccgacgagcagaaaaaaagaaagtaagttccattcctc  
 K T D E Q K K E S K F L P F L  
 598 accaacatcgaaactctatataacaacctgttggataacaagattgat  
 T N I E T L Y N N L V N K I D  
 643 gactacttaatcaacttgaaggcgaaaattaatgactgtacgac  
 D Y L I N L K A K I N D C N V  
 688 gaaaaggatgaagcccacgttaagatcaccaagcttccgatctc  
 E K D E A H V K I T K L S D L  
 733 aaagccatcgacgataagattgacctgtttaagaaccacaacgat  
 K A I D D K I D L F K N H N D  
 778 ttgcacgcaatcaaaaagttgatcaacgcacgataactaagaaagac  
 F D A I K K L I N D D T K K D  
 823 atgcttggaaaactgctgtcgacaggcttggccaaaactcccg  
 M L G K L L S T G L V Q N F P  
 868 aacaccattataagcaagctgatcgaaggaaagttcaggatatg

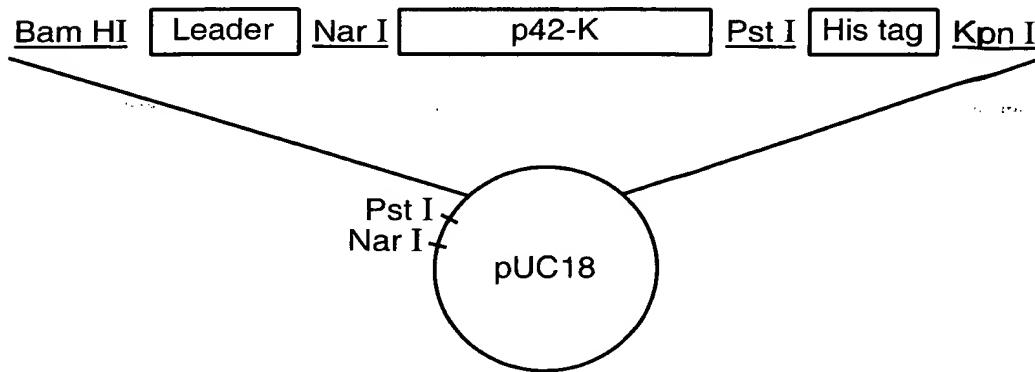


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N T I I S K L I E G K F Q D M  
 913 ctgaacatctctcagcatcaatgcgtgaagaagcaatgtcccgag  
 L N I S Q H Q C V K K Q C P E  
 958 aattcagggttgcctccgcacttagacgaaaggaggaaatgtaaa  
 N S G C F R H L D E R E E C K  
 1003 tgcctgctgaattataaacaggaaggagacaagtgcgttagagaat  
 C L L N Y K Q E G D K C V E N  
 1048 cctaaccacccaaacctgtaacgaaaaataacgggtggctgcgtgcac  
 P N P T C N E N N G G C D A D  
 1093 gctaagtgtaccgaggagcacagcggttccaatggcaagaaaata  
 A K C T E E D S G S N G K K I  
 1138 acttgcgaatgcacgaagcccgatagttaccctctttcgacggt  
 T C E C T K P D S Y P L F D G  
 1183 atcttctgctcc  
 I F C S

ccacacctcatcatcatcatcatcattaataaggtaaccta  
 P P H H H H H H \* \*

## FIG.\_ 12B



## FIG.\_ 13

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## DNA AND AMINO ACID SEQUENCE OF P42-K

1 GGATCCCT**AAA**ATGTGGAGCTGGAAGTGCCTCCTCTGGGCTGTCCTG  
 M W S W K C L L F W A V L

51 GTCACAGCCACACTCTGCACCGGCGCCGCAGTAACTCCTCCGTAAAT  
 V T A T L C T A G A A V T P S V I

101 TGATAACATACTTCTAAATTGAAAATGAATATGAGGTTTATATTAA  
 D N I L S K I E N E Y E V L Y L

151 AACCTTAGCAGGTGTTTAGAAGTTAAAAAAACAATTAGAAAATAAC  
 K P L A G V Y R S L K K Q L E N N

201 GTTATGACATTAAATGTTAATGTTAAGGATATTAAATTCACGATTAA  
 V M T F N V N V K D I L N S R F N

251 TAAACGTGAAAATTCAAAATGTTAGAATCAGATTAAATTCCATATA  
 K R E N F K N V L E S D L I P Y

301 AAGATTAAACATCAAGTAATTATGTTGTCAAAGATCCATATAAAATTCTT  
 K D L T S S N Y V V K D P Y K F L

351 AATAAAGAAAAAGAGATAAAATTCTTAAAGCAGTTATAATTATATTAAGGA  
 N K E K R D K F L S S Y N Y I K D

401 TTCAATAGATACGGATATAAATTGCAAATGATGTTCTGGATATTATA  
 S I D T D I N F A N D V L G Y Y

451 AAATATTATCCGAAAATATAAAATCAGATTAGATTCAATTAAAAAATAT  
 K I L S E K Y K S D L D S I K K Y

501 ATCAACGACAAACAAGGTGAAATGAGAAATACCTCCTTAAACAA  
 I N D K Q G E N E K Y L P F L N N

551 TATTGAGACCTTATAAAACAGTTAATGATAAAATTGATTTTAAGTAA  
 I E T L Y K T V N D K I D L F V

601 TTCATTAGAAGCAAAAGTTCTAAATTATACATATGAGAAATCAAACGTA  
 I H L E A K V L N Y T Y E K S N V

651 GAAGTTAAAAATAAAAGAACTTAATTACTTAAAAACAATTCAAGACAAATT  
 E V K I K E L N Y L K T I Q D K L

701 GGCAGATTTTAAAAAAATAACAATTTCGTTGGAATTGCTGATTTATCA  
 A D F K K N N N F V G I A D L S

751 CAGATTATAACCATAATAACTTATTGACAAAGTTCCTTAGTACAGGTATG  
 T D Y N H N N L L T K F L S T G M



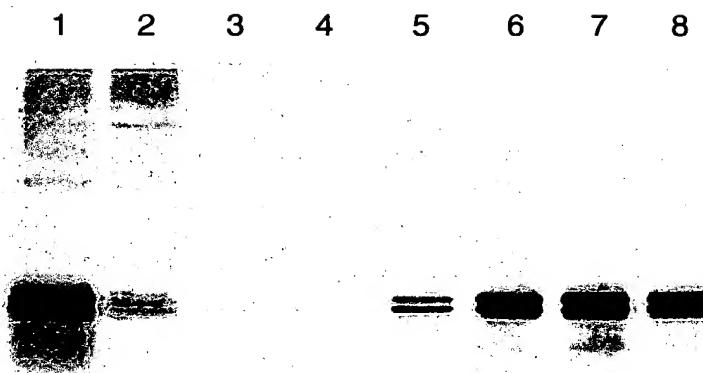
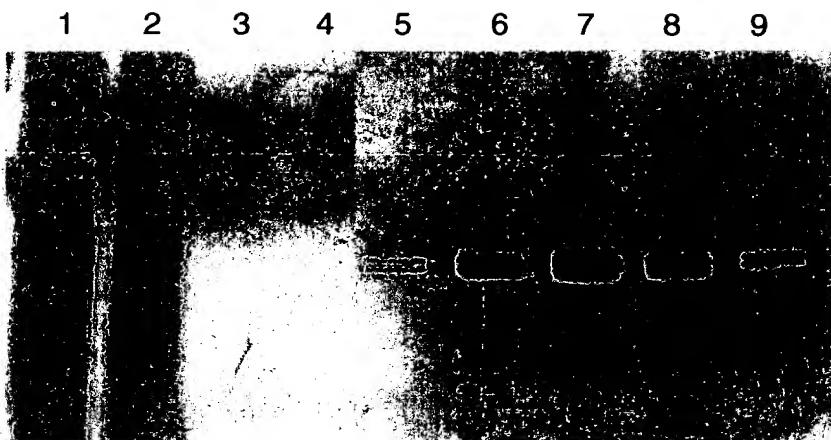
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801 GTTTTGAAAATCTGCTAAAACCGTTTATCTAATTTACTTGATGGAAA  
 V F E N L A K T V L S N L L D G N  
 851 CTTGCAAGGTATGTTAACATTCACAACACCAATGCGTAAAAAAACAAT  
 L Q G M L N I S Q H Q C V K K Q  
 901 GTCCACAAAATTCTGGATGTTCAGACATTTAGATGAAAGAGAAGAAATGT  
 C P Q N S G C F R H L D E R E E C  
 951 AAATGTTATTAAATTACAAACAAGAAGGTGATAAATGTGTTGAAATCC  
 K C L L N Y K Q E G D K C V E N P  
 1001 AAATCCTACTTGTAAACGAAAATAATGGTGGATGTGATGCAGATGCCAAAT  
 N P T C N E N N G G C D A D A K  
 1051 GTACCGAAGAAGATTCAAGGTAGCAACGGAAAGAAAATCACATGTGAATGT  
 C T E E D S G S N G K K I T C E C  
 1101 ACTAAACCTGATTCTTATCCACTTTGGTATTTCTGCAGTCATCA  
 T K P D S Y P L F D G I F C S H H  
 1151 TCATCATCATCATTAATAAGGTACC  
 H H H H \* \*

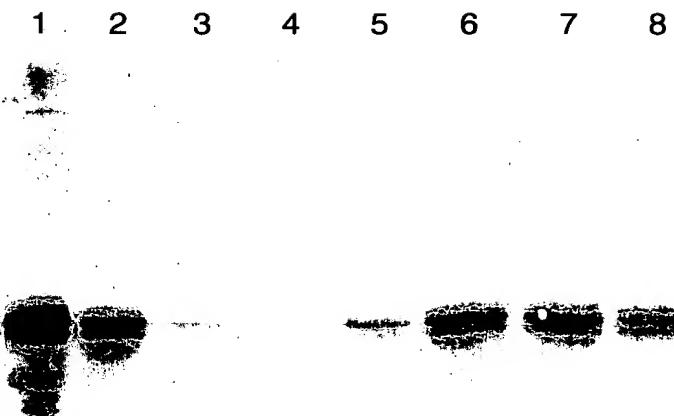
Underlined sequences represent restriction sites.  
 Bold letters represent alterations done to the leader sequence as described in the methods.  
 The boxed letter represents the original sequence where a mis-sense mutation to a cytosine occurred.  
 “\*” represent stop codons.

**FIG.\_ 14B**

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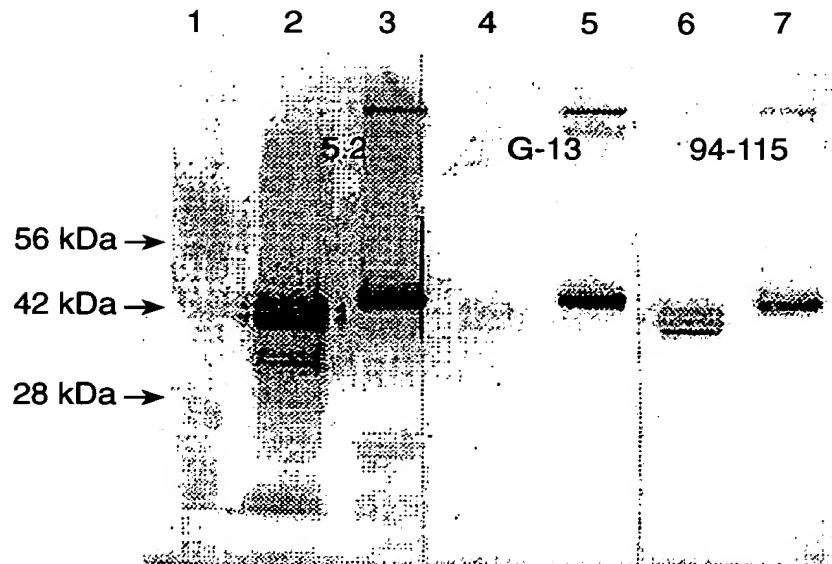
**FIG. 16**



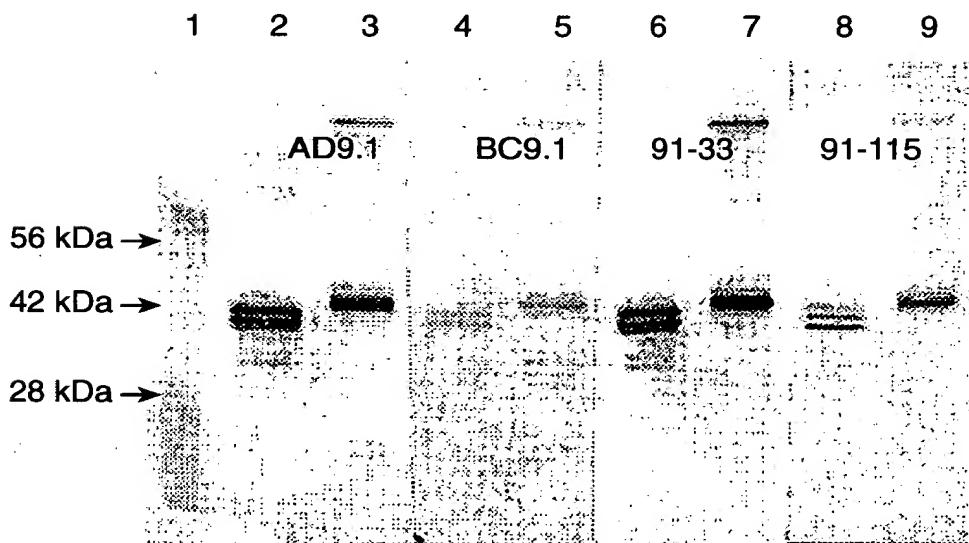
**FIG. 17**

17698 U.S. PTO  
102504

17698 U.S. PTO  
102504



**FIG.\_ 18A**



**FIG.\_ 18B**